

File No. 12-01/14-DC Pt.47
Central Drugs Standard Control Organization
Directorate General of Health Services
Ministry of Health & Family Welfare
FDA Bhawan, Kotla Road, New Delhi-110002

Dated: 03.07.2014

ORDER

SUBJECT: Procedure for review of applications of clinical trials and new drugs- renaming of New Drugs Advisory Committees (NDACs) - regarding

The Ministry of Health & Family Welfare had constituted an Expert Committee under the Chairmanship of Prof. Ranjit Roy Chaudhury to formulate policy and guidelines for approval of new drugs, clinical trials and banning of drugs. The Expert Committee submitted its report to the Ministry of Health & Family Welfare. The actions proposed to be taken on the recommendations of the Expert Committee were finalised by the Ministry of Health & Family Welfare.

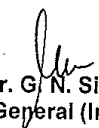
As per the action, New Drug Advisory Committees (NDACs) will be renamed as Subject Expert Committees. The members for their meetings will be drawn randomly from a large pool of experts. Applications of clinical trials and new drugs will initially be evaluated by the Subject Expert Committees and their recommendations will be reviewed by the Technical Review Committee (TRC). The TRC is proposed to be constituted under DGHS consisting of experts from each areas i.e. clinical pharmacology, regulatory clinical toxicology / pathology, medicinal / pharmaceutical chemistry, pharmacy and immunology including clinicians, basic scientists involved in drug development and subjects specialists (drug indication wise). CDSCO will grant approval of Clinical Trial and New Drugs based on the recommendations of TRC.

In pursuance to above, the twelve NDAC committees constituted vide order number X.19029/5/2011- DFQC dated 31.03.2011 are renamed as Subject Expert Committees (SEC) as under:

1. SEC- Oncology & hematology
2. SEC- Cardiovascular and renal
3. SEC- Metabolism & endocrinology
4. SEC- Antimicrobial, Antiparasitic & Antifungal, Antiviral
5. SEC- Reproductive & Urology
6. SEC- Gastroenterology & Hepatology
7. SEC- Dermatology & Allergy, immunology
8. SEC- Pulmonary
9. SEC- Neurology & Psychiatry
10. SEC- Analgesic, Anesthetics & Rheumatology
11. SEC- Ophthalmology
12. SEC- Vaccines

The terms of reference and other conditions will remain same.

Henceforth, in all correspondence related to evaluation of application of clinical trials, new drugs etc., the term Subject Expert Committee (SEC) as above should be used in place of NDAC.


(Dr. G. N. Singh)
Drugs Controller General (India)

- To
1. NDAC members
 2. IDMA / IPA / OPPI / ISCR / ACRO / FOPE / CIPI
 3. All officers of CDSCO

Copy to : US (D), MOH&FW, New Delhi.

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Dated: 03.07.2014


ORDER

**SUBJECT: Limiting Number of Clinical Trials an Investigator can undertake at a time-
regarding**

The Ministry of Health & Family Welfare had constituted an Expert Committee under the Chairmanship of Prof. Ranjit Roy Chaudhury to formulate policy and guidelines for approval of new drugs, clinical trials and banning of drugs. The Expert Committee submitted its report to the Ministry of Health & Family Welfare. The actions proposed to be taken on the recommendations of the Expert Committee were finalised by the Ministry of Health & Family Welfare.

Pursuant to above, it has been decided that the number of clinical trials an Investigator can undertake should be commensurate with the nature of the trial, facility available with the Investigator etc. However, under no circumstances the number of trials should be more than three at a time.

In view of above, all Sponsors / clinical trial applicants are hereby directed to ensure that the above recommendations are implemented and the Investigators are not involved in conduct of more than three clinical trials at a time.


(Dr. G. N. Singh)
Drugs Controller General (India)

To:

IDMA / IPA / OPPI / ISCR / ACRO

Copy to:

US (D), Ministry of Health and Family Welfare

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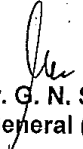
ORDER

SUBJECT: Clinical Trial on Medical Device- regarding

The Ministry of Health & Family Welfare had constituted an Expert Committee under the Chairmanship of Prof. Ranjit Roy Chaudhury to formulate policy and guidelines for approval of new drugs, clinical trials and banning of drugs. The Expert Committee submitted its report to the Ministry of Health & Family Welfare. The actions proposed to be taken on the recommendations of the Expert Committee were finalized by the Ministry of Health & Family Welfare.

Clinical Trial of Medical Device is different in nature as compared to that of Drugs or Vaccine. In case of Medical Device, there is no concept of conducting Phase I Clinical trial to assess safety, tolerability of the Medical Device. However, in pursuant to the decision of the Ministry of Health and Family Welfare, it has been decided that the procedures for the Clinical Trials approval, accreditations of Investigators, sites, Ethics Committee and such other conditions would be similar to the Clinical Trials of New Drugs/Vaccines

All concerned are hereby directed to comply with the above decision.


(Dr. G. N. Singh)
Drugs Controller General (India)

To:

1. IDMA / IPA / OPPI / ISCR / ACRO
2. NDAC / MDAC Members

CC to:

US(D), Ministry of Health and Family Welfare

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Central Drugs Standard Control Organization
Directorate General of Health Services
Ministry of Health & Family Welfare
FDA Bhawan, Kotla Road, New Delhi-110002

Dated: 03.07.2014


ORDER

SUBJECT: Clinical trial - Compensation in case of injury or death discerned at a later stage- regarding

The Ministry of Health & Family Welfare had constituted an Expert Committee under the Chairmanship of Prof. Ranjit Roy Chaudhury to formulate policy and guidelines for approval of new drugs, clinical trials and banning of drugs. The Expert Committee submitted its report to the Ministry of Health & Family Welfare. The actions proposed to be taken on the recommendations of the Expert Committee were finalized by the Ministry of Health & Family Welfare.

Pursuant to above, with regard to the compensation in case of injury or death discerned at a later stage, it has been decided that compensation in case of injury or death discerned at a later stage should be paid to the trial participant / his / her nominee as the case may be, if any drug-related anomaly is discerned at a later stage and accepted to be drug related.

In view of above, all Sponsors / Manufactures/Clinical Trial Applicants are hereby advised to provide compensation to the trial participant / his / her nominee as the case may be, if any drug-related anomaly is discerned at a later stage and accepted to be drug related injury or death.


(Dr. G. N. Singh)
Drugs Controller General (India)

To:

IDMA / IPA / OPPI / ISCR / ACRO

CC to: US(D), Ministry of Health and Family Welfare

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Directorate General of Health Services
Ministry of Health & Family Welfare
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ORDER

SUBJECT: Providing Ancillary care to the clinical trial subjects- regarding

The Ministry of Health & Family Welfare had constituted an Expert Committee under the Chairmanship of Prof. Ranjit Roy Chaudhury to formulate policy and guidelines for approval of new drugs, clinical trials and banning of drugs. The Expert Committee submitted its report to the Ministry of Health & Family Welfare. The actions proposed to be taken on the recommendations of the Expert Committee were finalised by the Ministry of Health & Family Welfare.

In pursuance to above, with regard to Providing Ancillary care to the clinical trial subjects, it has been decided that there should be provision for providing ancillary care to patients suffering from any other illness during the trial.

In view of above, all Sponsors / Manufactures/Clinical Trial Applicants are hereby advised that such ancillary care should be provided to the clinical trial subject for brief illness in the same hospital/trial site, wherever required.


(Dr. G. N. Singh)
Drugs Controller General (India)

To:

IDMA / IPA / OPPI / ISCR / ACRO

CC to: US (D), Ministry of Health and Family Welfare

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Central Drugs Standard Control Organization
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ORDER

SUBJECT: Approval of academic Clinical Trials- regarding

The Ministry of Health & Family Welfare had constituted an Expert Committee under the Chairmanship of Prof. Ranjit Roy Chaudhury to formulate policy and guidelines for approval of new drugs, clinical trials and banning of drugs. The Expert Committee submitted its report to the Ministry of Health & Family Welfare. The actions proposed to be taken on the recommendations of the Expert Committee were finalized by the Ministry of Health & Family Welfare.

In pursuance to above, it is stated that academic clinical research may be approved by the Institutional Ethics Committee (IEC). However, if a new drug is being evaluated or a new use for an existing drug is being evaluated, then approval of the DCGI is needed as per Drug & Cosmetic Rules.


(Dr. G. N. Singh)
Drugs Controller General (India)

To:

All Concerned / MCI / IMA

CC to: US (D), Ministry of Health and Family Welfare

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Ministry of Health & Family Welfare
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ORDER

**SUBJECT: Waiver of Clinical Trial in Indian population for approval of New Drugs-
regarding**

The Ministry of Health & Family Welfare had constituted an Expert Committee under the Chairmanship of Prof. Ranjit Roy Chaudhury to formulate policy and guidelines for approval of new drugs, clinical trials and banning of drugs. The Expert Committee submitted its report to the Ministry of Health & Family Welfare. The actions proposed to be taken on the recommendations of the Expert Committee were finalised by the Ministry of Health & Family Welfare.

In pursuance to above, it has been decided that waiver of Clinical Trial in Indian population for approval of new drugs, which have already been approved outside India, can presently be considered only in cases of national emergency, extreme urgency, and epidemic and for orphan drugs for rare diseases and drugs indicated for conditions/diseases for which there is no therapy.


(Dr. G. N. Singh)
Drugs Controller General (India)

To:

1. IDMA / IPA / OPPI / ISCR / ACRO
2. NDAC / MDAC Members

CC to:

US (D), Ministry of Health and Family Welfare

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ORDER

SUBJECT: Consideration of ethnicity for approval of new drugs- regarding

The Ministry of Health & Family Welfare had constituted an Expert Committee under the Chairmanship of Prof. Ranjit Roy Chaudhury to formulate policy and guidelines for approval of new drugs, clinical trials and banning of drugs. The Expert Committee submitted its report to the Ministry of Health & Family Welfare. The actions proposed to be taken on the recommendations of the Expert Committee were finalized by the Ministry of Health & Family Welfare.

In pursuance to above, in regard to the consideration of ethnicity for approval of new drugs, it has been decided that the following properties of a compound which make it more likely to be sensitive to ethnic factors shall be taken into consideration during evaluation of new drug applications:

- 1) Non-linear pharmacokinetics
- 2) A steep pharmacodynamic curve (a small change in dose results in a large change in effect) for both efficacy and safety in the range of the recommended dosage and dose regimen
- 3) A narrow therapeutic dose range
- 4) Highly metabolized, especially through a single pathway, thereby increasing the potential for drug-drug interaction
- 5) Metabolism by enzymes known to show genetic polymorphism
- 6) Administration as a prodrug, with the potential for ethnically variable enzymatic conversion
- 7) High inter-subject variation in bioavailability
- 8) Low bioavailability, thus more susceptible to dietary absorption effects
- 9) High likelihood of use in a setting of multiple-co-medications
- 10) High likelihood of inappropriate use, e.g. analgesics and tranquilizers.

It has also been decided that the following factors may be taken into consideration in deciding whether the available data could be ethnically sensitive or insensitive:

- 1) Definition of the disease and diagnosis of the patient
- 2) Choice of control group
- 3) Method of assessment of safety- Similarity of medical practice to the country of origin
- 4) Duration of trial
- 5) Regional medical practice of concomitant medication use
- 6) Severity distribution of eligible subjects
- 7) Similarity of dose and dosage regimen
- 8) Clinical end-point has to be acceptable to the region in assessing efficacy.

NDAC experts are therefore requested that applications for approval of new drugs should be evaluated keeping in view the above factors that may result in ethnic variations.


(Dr. G. N. Singh)
Drugs Controller General (India)

- To
1. IDMA / IPA / OPPI / ISCR / ACRO
 2. NDAC Members

CC to:

US (D), Ministry of Health and Family Welfare

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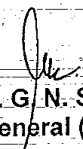
ORDER

SUBJECT: Requirements of local trial for a generics or similar biologics (Bio-similars) in other country like USA for its approval in the country-regarding

The Ministry of Health & Family Welfare had constituted an Expert Committee under the Chairmanship of Prof. Ranjit Roy Chaudhury to formulate policy and guidelines for approval of new drugs, clinical trials and banning of drugs. The Expert Committee submitted its report to the Ministry of Health & Family Welfare. The actions proposed to be taken on the recommendations of the Expert Committee were finalized by the Ministry of Health & Family Welfare.

In pursuance to above, in regard to consideration of requirements of local trial for a generics or similar biologics (Bio-similars) in other country like USA for its approval in the country, it has been decided that the drugs considered generics and similar biologics (biosimilars) in other countries like USA that have been marketed in such countries for more than four years and have a satisfactory report would be approved for marketing in India after abbreviated trials.

In view of above, all the NDAC experts are requested to evaluate applications of such new drugs which are considered generics and similar biologics (biosimilars) in other countries like USA are evaluated keeping in view the above requirements.


(Dr. G. N. Singh)
Drugs Controller General (India)

- To
1. NDAC Members
 2. IDMA / IPA / OPPI / ISCR / ACRO

CC to:

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ORDER

SUBJECT: Number of subjects in Phase III Global Clinical Trials - regarding

The Ministry of Health & Family Welfare had constituted an Expert Committee under the Chairmanship of Prof. Ranjit Roy Chaudhury to formulate policy and guidelines for approval of new drugs, clinical trials and banning of drugs. The Expert Committee submitted its report to the Ministry of Health & Family Welfare. The actions proposed to be taken on the recommendations of the Expert Committee were finalized by the Ministry of Health & Family Welfare.

Pursuant to above, it has been decided that if Indians have participated in Phase III Global Clinical Trials, the number of participants would have to be adequate for considering approval of the drug in India.

In view of above, all the NDAC experts are requested to evaluate applications of such new drugs NDAC adhering to the above said requirement.


(Dr. G. N. Singh)
Drugs Controller General (India)

- To
1. NDAC Members
 2. IDMA / IPA / OPPI / ISCR / ACRO

CC to:

US (D), Ministry of Health and Family Welfare

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Date:03.07.2014

ORDER

SUBJECT: Placebo controlled trials - regarding

The Ministry of Health & Family Welfare had constituted an Expert Committee under the Chairmanship of Prof. Ranjit Roy Chaudhury to formulate policy and guidelines for approval of new drugs, clinical trials and banning of drugs. The Expert Committee submitted its report to the Ministry of Health & Family Welfare. The actions proposed to be taken on the recommendations of the Expert Committee were finalized by the Ministry of Health & Family Welfare.

As mentioned in the report, Placebo-controlled trials are fairly uncommon these days, although there will always be a case for such trials in special circumstances. Since other remedies are usually available, the drug to be tested is compared to the existing therapy. There is thus no reason to deprive a patient of a drug in such placebo controlled trial. The pharmaceutical companies, the Investigators, the drugs regulator and the ECs all would have to ensure that the design used in a placebo controlled clinical trial is appropriate, efficient and ethical.

In view of the above, all the sponsors/CROs/Clinical trial applicants/Ethics Committees are required to ensure that the design used in a placebo controlled clinical trial is appropriate, efficient and ethical. The NDAC members are also requested to ensure that only those placebo control trials, design of which are appropriate, efficient and ethical considered for approval.


(Dr. G. N. Singh)
Drugs Controller General (India)

To

1. NDAC Members
2. IDMA / IPA / OPPI / ISCR / ACRO

CC to:

US (D), Ministry of Health and Family Welfare

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Date: 03.07.2014


ORDER

SUBJECT: Requirement for filing of application to market New Chemical Entities - regarding

The Ministry of Health & Family Welfare had constituted an Expert Committee under the Chairmanship of Prof. Ranjit Roy Chaudhury to formulate policy and guidelines for approval of new drugs, clinical trials and banning of drugs. The Expert Committee submitted its report to the Ministry of Health & Family Welfare. The actions proposed to be taken on the recommendations of the Expert Committee were finalized by the Ministry of Health & Family Welfare.

Pursuant to above, it has been decided that if Indian participates in global clinical trials of NCE(s) to be used for diseases that are prevalent in our population, after approval for marketing in the innovator country or in well-regulated developed country markets, approval should be sought from CDSCO for marketing these NCEs in India. After approval from CDSCO, these NCEs should be marketed in India speedily, preferably by production within the country.

All the sponsors / clinical trial applicants are hereby directed to provide an undertaking to CDSCO alongwith the application for approval of clinical trials of such New Chemical / Biological Entity that after approval for marketing of such entity in the innovator country or in well-regulated developed country, they will file application to CDSCO seeking approval for marketing such drugs in the country.


(Dr. G. N. Singh)
Drugs Controller General (India)

To
1. NDAC Members
2. IDMA / IPA / OPPI / ISCR / ACRO

CC to:

US (D), Ministry of Health and Family Welfare

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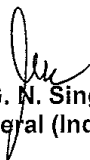
Date: 03.07.2014

ORDER

SUBJECT: Consideration of banning of a marketed drug - regarding

The Ministry of Health & Family Welfare had constituted an Expert Committee under the Chairmanship of Prof. Ranjit Roy Chaudhury to formulate policy and guidelines for approval of new drugs, clinical trials and banning of drugs. The Expert Committee submitted its report to the Ministry of Health & Family Welfare. The actions proposed to be taken on the recommendations of the Expert Committee were finalized by the Ministry of Health & Family Welfare.

In pursuance to the above, it has been decided that if two or more countries remove a drug from their market on grounds of efficacy and safety, then the continued marketing of the drug in the country will be considered for examination and appropriate action


(Dr. G. N. Singh)
Drugs Controller General (India)

To

IDMA / IPA / OPPI / FOPE / CIPI

CC to:

US (D), Ministry of Health and Family Welfare

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Directorate General of Health Services
Ministry of Health & Family Welfare
FDA Bhawan, Kotla Road, New Delhi-110002

Date: 03.07.2014

ORDER

SUBJECT: Creation of cell for co-ordination with institutes like ICMR for sponsoring various studies- regarding


The Ministry of Health & Family Welfare had constituted an Expert Committee under the Chairmanship of Prof. Ranjit Roy Chaudhury to formulate policy and guidelines for approval of new drugs, clinical trials and banning of drugs. The Expert Committee submitted its report to the Ministry of Health & Family Welfare. The actions proposed to be taken on the recommendations of the Expert Committee were finalized by the Ministry of Health & Family Welfare.

As per the report, the CDSCO may need information continuously on post-marketing Surveillance of drugs, rational use of medicines, drug utilization studies and adverse drug reaction monitoring etc. It will be useful if a research unit is created within the Central Drugs Standard Control Organization (CDSCO). This unit would initiate and sponsor studies in these areas to be able to get the needed information to help in decision-making.

Pursuant to the actions in this regard as decided by the Ministry, a cell is constituted in CDSCO comprising following officials to co-ordinate with agencies such as ICMR for the conduct of various studies.

- 1) Dr. A. Ramkishan , Deputy Drugs Controllers (India), CDSCO H.Q
- 2) Shri Somnath Basu, Asstt. Drugs Controller (India), CDSCO, H.Q
- 3) Shri. M. Balakumar, Drugs Inspector, CDSCO H.Q

The members of the cell will co-ordinate with agencies such as ICMR, for the conduct of specific studies for the Post-marketing surveillance of drugs, Rational use of medicines, Drug utilization studies, Adverse drug reaction monitoring etc. that would enable CDSCO for continued evaluation of drugs marketed in India and to take regulatory actions on continued use such drugs in the country.


(Dr. G. N. Singh)
Drugs Controller General (India)

To

All officers concerned / JDC (I), DDC (I), H.Q & Zonal officers

Copy to:

US (D), MOHFW, Nirman Bhawan, N. Delhi